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LISTING OF CLAIMS

1. (Cancelled) A method for identifying a mammalian tumor that responds to a HER2-directed therapy, wherein the mammalian tumor overexpresses HER2, the method comprising the step of assaying a sample obtained from the mammalian tumor to detect a pattern of expression, phosphorylation or both expression and phosphorylation of one or a plurality of polypeptides consisting of:
   (a) IGFR polypeptide;
   (b) EGFR polypeptide;
   (c) NDF polypeptide;
   (d) phosphorylated S6 ribosomal polypeptide;
   (e) phosphorylated AKT polypeptide; and
   (f) phosphorylated ERK polypeptide;
   wherein the detected pattern of expression, phosphorylation or both expression and phosphorylation identifies mammalian tumors that respond to a HER2-directed therapy.

2. (Cancelled) The method of claim 1, wherein the method comprises the step of assaying a sample obtained from the mammalian tumor to detect a pattern of expression, phosphorylation or both expression and phosphorylation of (a) IGFR polypeptide, and one or a plurality of polypeptides consisting of:
   (b) EGFR polypeptide;
   (c) NDF polypeptide;
   (d) phosphorylated S6 ribosomal polypeptide;
   (e) phosphorylated AKT polypeptide; and
   (f) phosphorylated ERK polypeptide.

3. (Cancelled) The method of claim 1, wherein the detected pattern is decreased expression of IGFR polypeptide in the mammalian tumor as compared to a non-tumor tissue or cell sample.

4. (Cancelled) The method of claim 1, wherein the detected pattern is normal or increased expression of IGFR polypeptide, accompanied by decreased phosphorylation of AKT

polypeptide, decreased phosphorylation of S6 ribosomal polypeptide or both in the mammalian tumor as compared to a non-tumor tissue or cell sample.

5. (Cancelled) The method of claim 1, wherein the detected pattern is normal or increased expression of EGFR polypeptide, accompanied by decreased phosphorylation of ERK polypeptide in the mammalian tumor as compared to a non-tumor tissue or cell sample.

6. (Cancelled) The method of claim 1, wherein the detected pattern is decreased expression of IGFR polypeptide, accompanied by increased phosphorylation of S6 ribosomal polypeptide in the mammalian tumor as compared to a non-tumor tissue or cell sample.

7. (Cancelled) The method of claim 1, wherein the detected pattern is decreased expression of IGFR polypeptide, accompanied by increased expression of NDF polypeptide in the mammalian tumor as compared to a non-tumor tissue or cell sample.

8. (Cancelled) The method of claim 6, wherein the detected pattern further includes increased phosphorylation of S6 ribosomal polypeptide

9. (Cancelled) A method for identifying a mammalian tumor that does not respond to a HER2-directed therapy, wherein the mammalian tumor overexpresses HER2, the method comprising the step of assaying a sample obtained from the mammalian tumor to detect a pattern of expression, phosphorylation or both expression and phosphorylation of one or a plurality of polypeptides consisting of:

(a) IGFR polypeptide;
(b) EGFR polypeptide;
(c) NDF polypeptide;
(d) phosphorylated S6 ribosomal polypeptide;
(e) phosphorylated AKT polypeptide; and
(f) phosphorylated ERK polypeptide;

wherein the detected pattern of expression, phosphorylation or both expression and phosphorylation identifies mammalian tumors that do not respond to HER2-directed therapy.

10. (Cancelled) The method of claim 9, wherein the method comprises the step of assaying a sample obtained from the mammalian tumor to detect a pattern of expression, phosphorylation or both expression and phosphorylation of (a) IGFR polypeptide, and one or a plurality of polypeptides consisting of:

(b) EGFR polypeptide;

(c) NDF polypeptide;

(d) phosphorylated S6 ribosomal polypeptide;

(e) phosphorylated AKT polypeptide; and

(f) phosphorylated ERK polypeptide.

11. (Cancelled) The method of claim 9, wherein the detected pattern is normal or increased expression of IGFR polypeptide, accompanied by increased phosphorylation of AKT polypeptide, increased phosphorylation of S6 ribosomal polypeptide, or both in the mammalian tumor as compared to a non-tumor tissue or cell sample.

12. (Cancelled) The method of claim 9, wherein the detected pattern is decreased expression of EGFR polypeptide and decreased expression of NDF polypeptide in the mammalian tumor as compared to a non-tumor tissue or cell sample.

13. (Cancelled) The method of claim 9, wherein the detected pattern is decreased expression of EGFR polypeptide in the mammalian tumor as compared to a non-tumor tissue or cell sample.

14. (Cancelled) The method of claim 9, wherein the detected pattern is decreased expression of NDF polypeptide in the mammalian tumor as compared to a non-tumor tissue or cell sample.

15. (Cancelled) The method of claim 9, wherein the detected pattern is decreased expression of EGFR polypeptide and increased phosphorylation of ERK polypeptide in the mammalian tumor as compared to a non-tumor tissue or cell sample.

16. (Cancelled) The method of claim 9, wherein the detected pattern is normal or increased expression of IGFR polypeptide and decreased expression of NDF in the mammalian tumor as compared to a non-tumor tissue or cell sample.

17. (Cancelled) The method of claim 1, wherein the detection of phosphorylation of AKT polypeptide, phosphorylation of S6 ribosomal polypeptide, or both is determined subsequent to contacting the sample obtained from the mammalian tumor with a HER2-directed therapy.

18. (Cancelled) The method of claim 4, wherein the detection of phosphorylation of AKT polypeptide, phosphorylation of S6 ribosomal polypeptide, or both is determined subsequent to contacting the sample obtained from the mammalian tumor with a HER2-directed therapy.

19. (Cancelled) The method of claim 9, wherein the detection of phosphorylation of AKT polypeptide, phosphorylation of S6 ribosomal polypeptide, or both is determined subsequent to contacting the sample obtained from the mammalian tumor with a HER2-directed therapy.

20. (Cancelled) The method of claim 11, wherein the detection of phosphorylation of AKT polypeptide, phosphorylation of S6 ribosomal polypeptide, or both is determined subsequent to contacting the sample obtained from the mammalian tumor with a HER2-directed therapy.

21. (Cancelled) The method of claim 1, wherein the HER2-directed therapy comprises rhuMAb HER2 (HERCEPTIN®).

22. (Cancelled) The method of claim 9, wherein the HER2-directed therapy comprises rhuMAb HER2 (HERCEPTIN®).

23. (Cancelled) The method of claim 1, wherein the sample obtained from the mammalian tumor has been contacted with at least one chemotherapeutic agent.

24. (Cancelled) The method of claim 9, wherein the sample obtained from the mammalian tumor has been contacted with at least one chemotherapeutic agent.

25. (Cancelled) The method of claim 1, wherein the detected pattern of expression, phosphorylation, or both, of one or a plurality of polypeptides (a) through (f) is determined using a biodetection reagent.

26. (Cancelled) The method of claim 25, wherein the biodetection reagent is an antibody.

27. (Cancelled) The method of claim 25, wherein the biodetection reagent is a nucleic acid probe.

28. (Cancelled) The method of claim 9, wherein the detected pattern of expression, phosphorylation, or both, of one or a plurality of polypeptides (a) through (f) is determined using a biodetection reagent.

29. (Cancelled) The method of claim 28, wherein the biodetection reagent is an antibody.

30. (Cancelled) The method of claim 28, wherein the biodetection reagent is a nucleic acid probe.

31. (Cancelled) The method of claim 1, wherein the detected pattern of phosphorylated AKT polypeptide is determined using an antibody specific for an epitope comprising a phosphorylated serine residue at position 473 in SEQ ID NO: 1.

32. (Cancelled) The method of claim 9, wherein the detected pattern of phosphorylated AKT polypeptide is determined using an antibody specific for an epitope comprising a phosphorylated serine residue at position 473 in SEQ ID NO: 1.

33. (Cancelled) The method of claim 1, wherein the detected pattern of phosphorylated S6 ribosomal polypeptide is determined using an antibody specific for an epitope comprising a phosphorylated serine residue at position 235 in SEQ ID NO: 2.

34. (Cancelled) The method of claim 9, wherein the detected pattern of phosphorylated S6 ribosomal polypeptide is determined using an antibody specific for an epitope comprising a phosphorylated serine residue at position 235 in SEQ ID NO: 2.

35. (Cancelled) The method of claim 1, wherein the detected pattern of phosphorylated ERK polypeptide is determined using an antibody specific for an epitope comprising a phosphorylated threonine residue at 202 or a phosphorylated serine residue at position 204 in SEQ ID NO: 3.

36. (Cancelled) The method of claim 9, wherein the detected pattern of phosphorylated ERK polypeptide is determined using an antibody specific for an epitope comprising a phosphorylated threonine residue at 202 or a phosphorylated serine residue at position 204 in SEQ ID NO: 3.

37. (Cancelled) The method of claim 1, wherein the sample obtained from the mammalian tumor is a paraffin-embedded biopsy sample.

38. (Cancelled) The method of claim 9, wherein the sample obtained from the mammalian tumor is a paraffin-embedded biopsy sample.

39. (Cancelled) The method of claim 1, wherein the mammalian tumor is identified as overexpressing HER2 using an antibody that binds HER2 polypeptide.

40. (Cancelled) The method of claim 9, wherein the mammalian tumor is identified as overexpressing HER2 using an antibody that binds HER2 polypeptide.

41. (Cancelled) A method of selecting a subject with cancer for treatment with a molecule targeting HER2, wherein the cancer overexpresses HER2, the method comprising the steps of:

(a) determining a pattern of expression, phosphorylation or both expression and phosphorylation in a cell or tissue sample from the subject of one or a plurality of polypeptides consisting of:

(i) IGFR polypeptide;

(ii) EGFR polypeptide;

(iii) NDF polypeptide;

(iv) phosphorylated S6 ribosomal polypeptide;

(v) phosphorylated AKT polypeptide; and

(vi) phosphorylated ERK polypeptide; and

(b) selecting the subject based on the detected pattern of expression, phosphorylation, or both expression and phosphorylation.

42. (Cancelled) The method of claim 41, wherein step (a) comprises determining a pattern of expression, phosphorylation or both expression and phosphorylation in a cell or tissue sample from the subject of (a) IGFR polypeptide, and one or a plurality of polypeptides consisting of:

(b) EGFR polypeptide;

(c) NDF polypeptide;

(d) phosphorylated S6 ribosomal polypeptide;

(e) phosphorylated AKT polypeptide; and

(f) phosphorylated ERK polypeptide.

43. (Cancelled) The method of claim 41, wherein the subject is selected when the detected pattern is decreased expression of IGFR polypeptide in the mammalian tumor as compared to a non-tumor tissue or cell sample.

44. (Cancelled) The method of claim 41, wherein the subject is selected when the detected pattern is normal or increased expression of IGFR polypeptide, accompanied by decreased phosphorylation of AKT polypeptide, decreased phosphorylation of S6

ribosomal polypeptide, or both in the mammalian tumor as compared to a non-tumor tissue or cell sample.

45. (Cancelled) The method of claim 41, wherein the subject is selected when the detected pattern is normal or increased expression of EGFR polypeptide, accompanied by decreased phosphorylation of ERK polypeptide in the mammalian tumor as compared to a non-tumor tissue or cell sample.

46. (Cancelled) The method of claim 41, wherein the subject is selected when the detected pattern is decreased expression of IGFR polypeptide, accompanied by increased phosphorylation of S6 ribosomal polypeptide in the mammalian tumor as compared to a non-tumor tissue or cell sample.

47. (Cancelled) The method of claim 41, wherein the subject is selected when the detected pattern is decreased expression of IGFR polypeptide, accompanied by increased expression of NDF polypeptide in the mammalian tumor as compared to a non-tumor tissue or cell sample.

48. (Cancelled) The method of claim 47, wherein the subject is selected when the detected pattern further includes increased phosphorylation of S6 ribosomal polypeptide

49. (Cancelled) The method of claim 41, wherein phosphorylation of AKT polypeptide, phosphorylation of S6 ribosomal polypeptide, or both is determined subsequent to contacting the sample obtained from the mammalian tumor with a HER2-directed therapy.

50. (Cancelled) The method of claim 44, wherein phosphorylation of AKT polypeptide, phosphorylation of S6 ribosomal polypeptide, or both is determined subsequent to contacting the sample obtained from the mammalian tumor with a HER2-directed therapy.

51. (Cancelled) The method of claim 41, wherein the HER2-directed therapy comprises rhuMAb HER2 (HERCEPTIN®).

52. (Cancelled) The method of claim 41, wherein the sample obtained from the mammalian tumor has been contacted with at least one chemotherapeutic.

53. (Cancelled) The method of claim 41, wherein the detected pattern of expression, phosphorylation, or both of one or a plurality of polypeptides (i) through (vi) is determined using a biodetection reagent.

54. (Cancelled) The method of claim 53, wherein the biodetection reagent is an antibody.

55. (Cancelled) The method of claim 53, wherein the biodetection reagent is a nucleic acid probe.

56. (Cancelled) The method of claim 41, wherein the detected pattern of phosphorylated AKT polypeptide is determined using an antibody specific for an epitope comprising a phosphorylated serine residue at position 473 in SEQ ID NO: 1.

57. The method of claim 41, wherein the detected pattern of phosphorylated S6 ribosomal polypeptide is determined using an antibody specific for an epitope comprising a phosphorylated serine residue at position 235 in SEQ ID NO: 2.

58. (Cancelled) The method of claim 41, wherein the detected pattern of phosphorylated ERK polypeptide is determined using an antibody specific for an epitope comprising a phosphorylated threonine residue at 202 or a phosphorylated serine residue at position 204 in SEQ ID NO: 3.

59. (Cancelled) The method of claim 41, wherein the cell or tissue sample from the subject is a paraffin-embedded biopsy sample.

60. (Cancelled) The method of claim 41, wherein the mammalian tumor is identified as overexpressing HER2 using an antibody that binds HER2 polypeptide.

61. (Cancelled) A method of selecting a subject with cancer to not receive treatment with a molecule targeting HER2, wherein the cancer overexpresses HER2, the method comprising the steps of:

(a) determining of a pattern of expression, phosphorylation, or both expression and phosphorylation in a cell or tissue sample from the subject of one or a plurality of polypeptides consisting of:

(i) IGFR polypeptide;

(ii) EGFR polypeptide;

(iii) NDF polypeptide;

(iv) phosphorylated S6 ribosomal polypeptide;

(v) phosphorylated AKT polypeptide;

(vi) phosphorylated ERK polypeptide; and

(b) selecting the subject based on the detected pattern of expression, phosphorylation, or both expression and phosphorylation.

62. (Cancelled) The method of claim 61, wherein step (a) comprises determining a pattern of expression, phosphorylation or both expression and phosphorylation in a cell or tissue sample from the subject of (a) IGFR polypeptide, and one or a plurality of polypeptides consisting of:

(b) EGFR polypeptide;

(c) NDF polypeptide;

(d) phosphorylated S6 ribosomal polypeptide;

(e) phosphorylated AKT polypeptide; and

(f) phosphorylated ERK polypeptide.

63. (Cancelled) The method of claim 61, wherein the subject is selected when wherein the detected pattern is normal or increased expression of IGFR polypeptide, accompanied by decreased phosphorylation of AKT polypeptide, decreased phosphorylation of S6 ribosomal polypeptide, or both in the mammalian tumor as compared to a non-tumor tissue or cell sample.

64. (Cancelled) The method of claim 61, wherein the subject is selected wherein the detected pattern is decreased expression of EGFR polypeptide and decreased expression of NDF polypeptide in the mammalian tumor as compared to a non-tumor tissue or cell sample.

65. (Cancelled) The method of claim 61, wherein the subject is selected when the detected pattern is decreased expression of EGFR polypeptide in the mammalian tumor as compared to a non-tumor tissue or cell sample.

66. (Cancelled) The method of claim 61, wherein the subject is selected when the detected pattern is decreased expression of NDF polypeptide in the mammalian tumor as compared to a non-tumor tissue or cell sample.

67. (Cancelled) The method of claim 61, wherein the subject is selected when the detected pattern is decreased expression of EGFR polypeptide and increased phosphorylation of ERK polypeptide in the mammalian tumor as compared to a non-tumor tissue or cell sample.

68. (Cancelled) The method of claim 61, wherein the subject is selected when the detected pattern is normal or increased expression of IGFR polypeptide and decreased expression of NDF in the mammalian tumor as compared to a non-tumor tissue or cell sample.

69. (Cancelled) The method of claim 61, wherein phosphorylation of AKT polypeptide, phosphorylation of S6 ribosomal polypeptide, or both is determined subsequent to contacting the sample obtained from the mammalian tumor with a HER2-directed therapy.

70. (Cancelled) The method of claim 63, wherein phosphorylation of AKT polypeptide, phosphorylation of S6 ribosomal polypeptide, or both is determined subsequent to contacting the sample obtained from the mammalian tumor with a HER2-directed therapy.

71. (Cancelled) The method of claim 61, wherein the HER2-directed therapy comprises rhuMAb HER2 (HERCEPTIN®).

72. (Cancelled) The method of claim 61, wherein the sample obtained from the mammalian tumor has been contacted with at least one chemotherapeutic.

73. (Cancelled) The method of claim 61, wherein the detected pattern of expression, phosphorylation, or both of one or a plurality of polypeptides (i) through (vi) is determined using a biodetection reagents.

74. (Cancelled) The method of claim 73, wherein the biodetection reagent is an antibody.

75. (Cancelled). The method of claim 73, wherein the biodetection reagent is a nucleic acid probe.

76. (Cancelled) The method of claim 61, wherein the detected pattern of phosphorylated AKT polypeptide is determined using an antibody specific for an epitope comprising a phosphorylated serine residue at position 473 in SEQ ID NO: 1.

77. (Cancelled) The method of claim 61, wherein the detected pattern of phosphorylated S6 ribosomal polypeptide is determined using an antibody specific for an epitope comprising a phosphorylated serine residue at position 235 in SEQ ID NO: 2.

78. (Cancelled) The method of claim 61, wherein the detected pattern of phosphorylated ERK polypeptide is determined using an antibody specific for an epitope comprising a phosphorylated threonine residue at 202 or a phosphorylated serine residue at position 204 in SEQ ID NO: 3.

79. (Cancelled) The method of claim 61, wherein the cell or tissue sample is a paraffin-embedded biopsy sample.

80. (Cancelled) The method of claim 61, wherein the mammalian tumor is identified as overexpressing HER2 using an antibody that binds HER2 polypeptide.

81. (Cancelled) A kit for characterizing a mammalian tumor's responsiveness to a HER2-directed therapy, the kit comprising:

(a) an antibody that binds IGFR polypeptide,

and one or more of the following:

(b) an antibody that binds phosphorylated AKT polypeptide;

(c) an antibody that binds phosphorylated S6 ribosomal polypeptide;

(d) an antibody that binds EGFR polypeptide;

(e) an antibody that binds HER2 polypeptide;

(f) an antibody that binds NDF polypeptide; and

(g) an antibody that binds phosphorylated ERK polypeptide.

82. (Cancelled) The kit of claim 81, wherein the antibody of (b) is immunologically specific for AKT polypeptide having a phosphorylated serine residue at position 473 in SEQ ID NO: 1; antibody of (c) is immunologically specific for S6 ribosomal polypeptide having a phosphorylated serine residue at position 235 in SEQ ID NO: 2; and/or antibody of (f) is immunologically specific for EKT polypeptide having a phosphorylated threonine residue at position 202 and a phosphorylated tyrosine at position 204 in SEQ ID NO: 3.

83. (Cancelled) The kit of claim 81, wherein the kit further comprises at least one secondary antibody that binds to an antibody of subpart (a) through (g).

84. (Currently Amended) A method for identifying a HER-2 over-expressing mammalian tumor that is likely to respond to a HER-2 directed therapy, the method comprising the steps of:

(i) assaying a sample obtained from the mammalian tumor to detect a pattern of ~~expression and/or phosphorylation of~~:

(a) phosphorylation of an S6 ribosomal polypeptide ~~expression of a NDF (Heregulin) polypeptide~~;

(b) expression of an IGFR (Insulin-like Growth Factor Receptor) polypeptide; and optionally

(c) expression of a NDF (Heregulin) polypeptide; and ~~phosphorylated S6 ribosomal polypeptide~~

(ii) comparing said pattern to a pattern detected in a sample obtained from a non-tumor tissue or cell sample, wherein a change in the detected pattern ~~of expression and/or phosphorylation~~ identifies ~~whether~~ said mammalian tumor ~~is~~ as likely to respond to a HER-2 directed therapy.

85. (Currently Amended) The method of claim 84, wherein the detected pattern is ~~decreased~~ increased phosphorylation ~~expression~~ of S6 ribosomal ~~NDF~~ polypeptide, accompanied by ~~increased~~ decreased expression of IGFR polypeptide in the mammalian tumor as compared to ~~a~~ said non-tumor tissue or cell sample, wherein said pattern identifies said tumor as ~~not~~ likely to respond to a HER-2 directed therapy.

86. (Previously Presented) The method of claim 84, wherein the detected pattern is increased expression of NDF polypeptide, accompanied by increased phosphorylation of S6 ribosomal polypeptide and decreased expression of IGFR polypeptide in the mammalian tumor as compared to a non-tumor tissue or cell sample, wherein said pattern identifies said tumor as likely to respond to a HER-2 directed therapy.

87. (Currently Amended) The method of claim 84, wherein the detected pattern of ~~phosphorylated~~ phosphorylation of S6 ribosomal polypeptide is determined using an antibody specific for an epitope comprising a phosphorylated serine residue at position 235 in SEQ ID NO: 2.

88. (Currently Amended) The method of claim ~~1~~ 84, wherein said mammalian tumor is a breast tumor.

89. (Currently Amended) A method for identifying a HER-2 over-expressing mammalian tumor that is likely to respond to a HER-2 directed therapy, the method comprising the steps of:

(i) assaying a sample obtained from the mammalian tumor to detect a pattern of expression ~~and/~~ or phosphorylation of two or more polypeptides selected from the group consisting of:

(a) expression of an IGFR (Insulin-like Growth Factor Receptor) polypeptide;

(b) ~~phosphorylated~~ phosphorylation of an S6 ribosomal polypeptide;

(c) expression of a NDF (Heregulin) polypeptide;

(d) expression of an EGFR (Epidermal Growth Factor Receptor) polypeptide;

(e) ~~phosphorylated~~ phosphorylation of an AKT polypeptide; and

(f) ~~phosphorylated~~ phosphorylation of an ERK polypeptide; to establish a first detected pattern and

(ii) comparing said pattern to a pattern detected in a sample obtained from a non-tumor tissue or cell sample, wherein a change in the detected pattern ~~of expression and/or phosphorylation~~ identifies ~~whether~~ said mammalian tumor ~~is~~ as likely to respond to a HER-2 directed therapy.

90. (Previously Presented) The method of claim 89, wherein the detected pattern is increased expression of NDF polypeptide, accompanied by increased phosphorylation of S6 ribosomal polypeptide and decreased expression of IGFR polypeptide in the mammalian tumor as compared to a non-tumor tissue or cell sample, wherein said pattern identifies said tumor as likely to respond to a HER-2 directed therapy.

91. (Previously Presented) The method of claim 89, wherein the detected pattern is decreased expression of NDF polypeptide, accompanied by increased expression of IGFR polypeptide in the mammalian tumor as compared to a non-tumor tissue or cell sample, wherein said pattern identifies said tumor as not likely to respond to a HER-2 directed therapy.

92. (Previously Presented) The method of claim 89, wherein the detected pattern is decreased expression of NDF polypeptide, accompanied by a decrease in phosphorylation of the S6 ribosomal polypeptide and decreased expression of IGFR polypeptide and in the mammalian tumor as compared to a non-tumor tissue or cell sample, wherein said pattern identifies said tumor as not likely to respond to a HER-2 directed therapy.

93. (Previously Presented) The method of claim 89, wherein the detected pattern is decreased expression of NDF polypeptide, accompanied by decreased expression of EGFR polypeptide in the mammalian tumor as compared to a non-tumor tissue or cell sample, wherein said pattern identifies said tumor as not likely to respond to a HER-2 directed therapy.

94. (Previously Presented) The method of claim 89, wherein the detected pattern is decreased expression of NDF polypeptide, accompanied by increased phosphorylation of ERK polypeptide and increased expression of EGFR polypeptide in the mammalian tumor as

compared to a non-tumor tissue or cell sample, wherein said pattern identifies said tumor as not likely to respond to a HER-2 directed therapy.

95. (Previously Presented) The method of claim 89, wherein the detected pattern is increased expression of NDF polypeptide, accompanied by increased phosphorylation of ERK polypeptide and decreased expression of EGFR polypeptide in the mammalian tumor as compared to a non-tumor tissue or cell sample, wherein said pattern identifies said tumor as not likely to respond to a HER-2 directed therapy.

96. (Previously Presented) The method of claim 89, wherein the detected pattern is decreased expression of EGFR polypeptide, accompanied by increased phosphorylation of ERK polypeptide in the mammalian tumor as compared to a non-tumor tissue or cell sample, wherein said pattern identifies said tumor as not likely to respond to a HER-2 directed therapy.

97. (Previously Presented) The method of claim 89, wherein the detected pattern is decreased expression of EGFR polypeptide, accompanied by decreased phosphorylation of AKT polypeptide in the mammalian tumor as compared to a non-tumor tissue or cell sample, wherein said pattern identifies said tumor as not likely to respond to a HER-2 directed therapy.

98. (Previously Presented) The method of claim 89, wherein the detected pattern is increased expression of IGFR polypeptide, accompanied by increased phosphorylation of S6 ribosomal polypeptide in the mammalian tumor as compared to a non-tumor tissue or cell sample, wherein said pattern identifies said tumor as not likely to respond to a HER-2 directed therapy.

99. (Previously Presented) The method of claim 89, wherein the detected pattern of expression and phosphorylation or both expression and phosphorylation is determined subsequent to contacting the sample obtained from the mammalian tumor with a HER-2 directed therapy.

100. (Previously Presented) The method of claim 89, wherein the HER2-directed therapy comprises rhuMAb HER-2.

101. (Presently Amended) The method of claim 89, wherein the detected pattern of expression, or phosphorylation, ~~or both,~~ of one or a plurality of polypeptides (a) through (f) of

steps (i) and (ii) are ~~is~~ determined using an antibody, a nucleic acid probe, and/or a peptide probe.

102. (Previously Presented) The method of claim 89, wherein the detected pattern of phosphorylated AKT polypeptide is determined using an antibody specific for an epitope comprising a phosphorylated serine residue at position 473 in SEQ ID NO: 1.

103. (Previously Presented) The method of claim 89, wherein the detected pattern of phosphorylated S6 ribosomal polypeptide is determined using an antibody specific for an epitope comprising a phosphorylated serine residue at position 235 in SEQ ID NO: 2.

104. (Previously Presented) The method of claim 89, wherein the detected pattern of phosphorylated ERK polypeptide is determined using an antibody specific for an epitope comprising a phosphorylated threonine residue at 202 or a phosphorylated serine residue at position 204 in SEQ ID NO: 3.

105. (Previously Presented) The method of claim 89, wherein the sample obtained from the mammalian tumor is a paraffin-embedded biopsy sample.

106. (Previously Presented) The method of claim 89, wherein the mammalian tumor is identified as overexpressing HER-2 using an antibody that binds HER-2 polypeptide.

107. (Previously Presented) The method of claim 89, wherein said mammalian tumor is a breast tumor.

108. (Previously Presented) A kit for identifying a mammalian tumor that is likely to respond to a HER2-directed therapy, the kit comprising:

(a) an antibody that binds HER-2 polypeptide, and one or more of the following:

(b) an antibody that binds phosphorylated AKT polypeptide;

(c) an antibody that binds phosphorylated S6 ribosomal polypeptide;

(d) an antibody that binds EGFR polypeptide;

(e) an antibody that binds HER2 polypeptide;

(f) an antibody that binds NDF polypeptide; and

(g) an antibody that binds phosphorylated ERK polypeptide.

109. (Previously Presented) The kit of claim 108, wherein the antibody of (b) is specific for AKT polypeptide having a phosphorylated serine residue at position 473 in SEQ ID NO: 1; wherein the antibody of (c) is specific for S6 ribosomal polypeptide having a phosphorylated serine residue at position 235 in SEQ ID NO: 2; and/or antibody of (f) is specific for EKT polypeptide having a phosphorylated threonine residue at position 202 and a phosphorylated tyrosine at position 204 in SEQ ID NO: 3.

110. (Previously Presented) The kit of claim 108, wherein the kit further comprises at least one secondary antibody that binds to an antibody of subpart (a) through (g).

111. (New) The method of claim 84, wherein the HER2-directed therapy comprises rhuMAb HER-2.

112. (New) The method of claim 84, wherein the sample obtained from the mammalian tumor is a paraffin-embedded biopsy sample.

113. (New) The method of claim 84, wherein the mammalian tumor is identified as overexpressing HER-2 using an antibody that binds HER-2 polypeptide.